CLAIMS:

- 1. A method for the treatment of accelerated bone resorption in a mammal subject, the method comprises administering to said subject in need of said treatment an amount of an A₃ adenosine receptor agonist (A₃AR agonist), the amount being effective to inhibit bone resorption.
- 2. The method of Claim 1, wherein said mammal is a human subject.
- 3. The method of Claim 1, for the treatment of inflammation induced bone resorption.
- 4. The method of Claim 3, for the treatment of bone resorption induced by inflammatory arthritis.
- 5. The method of Claim 1, wherein said treatment comprises oral administration of A₃AR agonist to said subject in need.
- 6. The method of Claim 5, wherein said treatment comprises administration of A₃RA agonist to said subject once or twice daily.
- 7. The method of Claim 1, wherein said A_3AR agonist is a compound within the scope of the general formula (I):

$$R_3$$
 R_1
 R_2
 R_1
 R_2

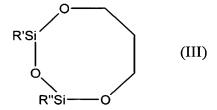
wherein,

- R_1 represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):

$$X_1$$
 Y X_2 X_3 X_4 X_4

in which:

- Y represents an oxygen, sulfur or CH₂;
- X₁ represents H, alkyl, R^aR^bNC(=O)- or HOR^c-, wherein
 - R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and
 - R^c is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;
- X_2 is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;
- X_3 and X_4 represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both X_3 and X_4 are oxygens connected to >C=S to form a 5-membered ring, or X_2 and X_3 form the ring of formula (III):



where R' and R" represent independently an alkyl group;

- R_2 is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl; alkynyl, thio, and alkylthio; and
 - R_3 is a group of the formula $-NR_4R_5$ wherein
- \mathbf{R}_4 is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with \mathbf{Z} being O, S, or NR^a with \mathbf{R}^a having the above meanings; wherein when \mathbf{R}_4 is hydrogen than
- R_5 is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo,

haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl- aminobenzyl, β -alanylaminobenzyl, T-BOC- β -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or R_5 is a group of the following formula:

or when $\mathbf{R_4}$ is an alkyl or aryl-NH-C(Z)-, then, $\mathbf{R_5}$ is selected from the group consisting of heteroaryl-NR^a-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR^a-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; \mathbf{Z} representing an oxygen, sulfor or amine; or a physiologically acceptable salt of the above compound.

8. The method of claim 1, wherein said A_3AR agonist is a nucleoside derivative of the general formula (IV):

wherein X_1 , R_2 and R_4 are as defined in claim 3, and physiologically acceptable salts of said compound.

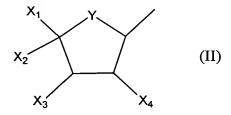
- 9. The method of Claim 1 wherein said A₃AR agonist is selected from N⁶-2- (4-aminophenyl)ethyladenosine (APNEA), N⁶-(4-amino-3-iodobenzyl) adenosine- 5'-(N-methyluronamide) (AB-MECA), N⁶-(3-iodobenzyl)-adenosine-5'-N-methyluronamide (IB-MECA) and 2-chloro-N⁶-(3-iodobenzyl)- adenosine-5'-N-methyluronamide (Cl-IB-MECA).
- 10. The method of claim 9, wherein said A_3AR agonist is IB-MECA.

- 11. A pharmaceutical composition for the treatment of accelerated bone resorption, the composition comprising an amount of an A_3AR agonist, the amount being effective to inhibit bone resorption in a mammal subject.
- 12. The pharmaceutical composition of Claim 11, in a dosage form suitable for oral administration.
- 13. The pharmaceutical composition of Claim 11, for the treatment of inflammation induced bone resorption.
- 14. The pharmaceutical composition of Claim 13, for the treatment of bone resorption induced by inflammatory arthritis.
- 15. The pharmaceutical composition of Claim 11, wherein said A_3AR agonist is a compound within the scope of the general formula (I):

$$R_1$$
 R_2 R_3 R_2 R_2

wherein,

- R_1 represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):

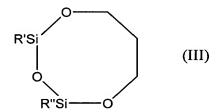


in which:

- Y represents an oxygen, sulfur or CH₂;
- X₁ represents H, alkyl, R^aR^bNC(=O)- or HOR^c-, wherein
 - $\mathbf{R}^{\mathbf{a}}$ and $\mathbf{R}^{\mathbf{b}}$ may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl,

BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and

- R^c is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;
- X₂ is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;
- X_3 and X_4 represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both X_3 and X_4 are oxygens connected to >C=S to form a 5-membered ring, or X_2 and X_3 form the ring of formula (III):



where R' and R" represent independently an alkyl group;

- R_2 is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl; alkynyl, thio, and alkylthio; and
 - R_3 is a group of the formula $-NR_4R_5$ wherein
- \mathbf{R}_4 is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with \mathbf{Z} being O, S, or NR^a with \mathbf{R}^a having the above meanings; wherein when \mathbf{R}_4 is hydrogen than
- R₅ is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo, haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl- aminobenzyl, β-alanylaminobenzyl, T-BOC-β-alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or R₅ is a group of the following formula:

$$- \sqrt{\frac{1}{N}} \sqrt{\frac{N}{N}} \sqrt{\frac{N}{$$

or when \mathbf{R}_4 is an alkyl or aryl-NH-C(Z)-, then, \mathbf{R}_5 is selected from the group consisting of heteroaryl-NR^a-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR^a-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; \mathbf{Z} representing an oxygen, sulfor or amine; or a physiologically acceptable salt of the above compound.

16. The pharmaceutical composition of Claim 11, wherein said A_3AR agonist is a nucleoside derivative of the general formula (IV):

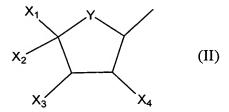
wherein X_1 , R_2 and R_4 are as defined in claim 3, and physiologically acceptable salts of said compound.

- 17. The pharmaceutical composition of Claim 11, wherein said A_3AR agonist is selected from N^6 -2- (4-aminophenyl)ethyladenosine (APNEA), N^6 -(4-amino-3-iodobenzyl) adenosine- 5'-(N-methyluronamide) (AB-MECA), N^6 -(3-iodobenzyl)-adenosine-5'-N- methyluronamide (IB-MECA) and 2-chloro- N^6 -(3-iodobenzyl)- adenosine-5'-N-methyluronamide (Cl-IB-MECA).
- 18. The pharmaceutical composition of Claim 11, wherein said A₃AR agonist is IB-MECA.
- 19. Use of an A₃AR agonist for the preparation of a pharmaceutical composition for the treatment of accelerated bone resorption.

- **20.** The use of Claim 19, for the preparation of a composition suitable for oral administration.
- 21. The use of Claim 20, for the preparation of a composition the treatment of inflammation induced bone resorption.
- 22. The use of Claim 21, wherein said composition is for the treatment of bone resorption induced by inflammatory arthritis.
- 23. The use of Claim 19, wherein said A_3AR agonist is a compound within the scope of the general formula (I):

wherein,

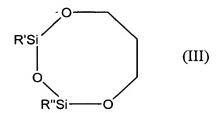
- R_1 represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):



in which:

- Y represents an oxygen, sulfur or CH₂;
- X_1 represents H, alkyl, $R^aR^bNC(=0)$ or HOR^c -, wherein
 - R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and
 - R^c is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;

- X₂ is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;
- X_3 and X_4 represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both X_3 and X_4 are oxygens connected to >C=S to form a 5-membered ring, or X_2 and X_3 form the ring of formula (III):



where R' and R" represent independently an alkyl group;

- R_2 is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl; alkynyl, thio, and alkylthio; and
 - R₃ is a group of the formula –NR₄R₅ wherein
- \mathbf{R}_4 is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with \mathbf{Z} being O, S, or NR^a with \mathbf{R}^a having the above meanings; wherein when \mathbf{R}_4 is hydrogen than
- R_5 is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo, haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl- aminobenzyl, β -alanylaminobenzyl, T-BOC- β -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or R_5 is a group of the following formula:

or when R_4 is an alkyl or aryl-NH-C(Z)-, then, R_5 is selected from the group consisting of heteroaryl-NR^a-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR^a-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; **Z** representing an oxygen, sulfor or amine; or a physiologically acceptable salt of the above compound.

24. The use of Claim 19, wherein said A_3AR agonist is a nucleoside derivative of the general formula (IV):

$$R_4$$
NH
NH
N
 R_2
(IV)

wherein X_1 , R_2 and R_4 are as defined in claim 3, and physiologically acceptable salts of said compound.

- 25. The use of Claim 19, wherein said A_3AR agonist is selected from N^6 -2-(4-aminophenyl)ethyladenosine (APNEA), N^6 -(4-amino-3-iodobenzyl) adenosine- 5'-(N-methyluronamide) (AB-MECA), N^6 -(3-iodobenzyl)-adenosine-5'-N- methyluronamide (IB-MECA) and 2-chloro- N^6 -(3-iodobenzyl)- adenosine-5'-N-methyluronamide (Cl-IB-MECA).
- 26. The use of Claim 19, wherein said A_3AR agonist is IB-MECA.